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STENT WITH ECCENTRIC COATING

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of pending United States Provisional Patent Application No. 60/420,773, filed October 22, 2002, the priority of which is hereby claimed.

TECHNICAL FIELD

[0002] The technical field of this disclosure is medical implant devices, particularly, coated stents.

BACKGROUND OF THE INVENTION

[0003] Stents are generally cylindrical shaped devices that are radially expandable to hold open a segment of a blood vessel or other anatomical lumen after implantation into the body lumen. Stents have been developed with coatings to deliver drugs or other therapeutic agents.

[0004] Stents are used in conjunction with balloon catheters in a variety of medical therapeutic applications including intravascular angioplasty. For example, a balloon catheter device is inflated during PTCA (percutaneous transluminal coronary angioplasty) to dilate a stenotic blood vessel. The stenosis may be the result of a lesion comprised of, for example, a plaque or thrombus. After inflation, the pressurized balloon exerts a compressive force on the lesion thereby increasing the inner diameter of the affected vessel. The increased interior vessel diameter facilitates improved blood flow. Soon after the procedure, however, in a significant number of cases treated vessels re-narrow.

[0005] To reduce occurrence of restenosis, short flexible cylinders, or stents, constructed of metal or various polymers are implanted within the vessel to maintain lumen size. The stents act as a scaffold to support the lumen in an open position. Various configurations of stents include a cylindrical tube defined by a mesh, interconnected stents or like segments. Some exemplary

stents are disclosed in U.S. Patent No. 5,292,331 to Boneau, U.S. Patent No. 6,090,127 to Globerman, U.S. Patent No. 5,133,732 to Wiktor, U.S. Patent No. 4,739,762 to Palmaz and U.S. Patent No. 5,421,955 to Lau. Balloon-expandable stents are mounted on a collapsed balloon at a diameter smaller than when the stents are deployed. Stents can also be self-expanding, growing to a final diameter when deployed without mechanical assistance from a balloon or like device.

[0006] Stents have been used with coatings to deliver drug or other therapy at the site of the stent. The coating may also be passive. The coating can be applied as a liquid containing the drug or other therapeutic agent dispersed in a polymer/solvent matrix. The liquid coating then dries to a solid coating upon the stent. The liquid coating can be applied by dipping or spraying the stent while spinning or shaking the stent to achieve a uniform coating. Combinations of the various application techniques can also be used.

[0007] The purpose of the coating is to deliver the drug to the tissue adjacent to the stent, such as the interior wall of an artery or vessel. Therefore, it is most important that the drug be present on at least the outer diameter of the stent. The coating has generally been applied uniformly over the inside and outside diameters of the stent, in one or more layers over the stent wires. Because drugs to reduce the occurrence of restenosis are only required at the stent outer diameter where the stent contacts the vessel tissue and not at the stent inner diameter containing blood, applying a drug-containing coating uniformly can lead to adverse drug effects or delivery to non-target tissue. For example, a drug on the inner diameter can flow into the blood where it is not beneficial. In addition, some drugs and polymers require a certain quantity or concentration before an effective therapy can be delivered. A uniform coating of a thickness necessary to provide sufficient drug at the outer diameter of the stent to constitute an effective therapy may interfere with blood flow through the inner lumen of the stent.

[0008] It would be desirable to have a stent having an eccentric coating that would overcome the above disadvantages.

SUMMARY OF THE INVENTION

[0009] One aspect of the present invention provides a stent having an eccentric coating to target drug delivery to tissue at the outer diameter of the stent.

[0010] Another aspect of the present invention provides a stent having an eccentric coating to avoid drug waste.

[0011] Another aspect of the present invention provides a stent having an eccentric coating to reduce drug delivery to the blood.

[0012] Another aspect of the present invention provides a stent having an eccentric coating able to provide different characteristics and therapies at the vessel wall and lumen sides.

[0013] The foregoing and other features and advantages of the invention will become further apparent from the following detailed description of the presently preferred embodiments, read in conjunction with the accompanying drawings. The detailed description and drawings are merely illustrative of the invention, rather than limiting the scope of the invention being defined by the appended claims and equivalents thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] **FIG. 1** shows a stent delivery system made in accordance with the present invention.

[0015] **FIGS. 2 & 3** show a stent and a cross section, respectively, of a coated stent made in accordance with the present invention.

[0016] **FIGS. 4A, 4B, 4C** and **4D** show various cross-sections of stent wires with eccentric coatings made in accordance with the present invention.

[0017] **FIG. 5** shows a method of manufacturing a coated stent made in accordance with the present invention.

[0018] **FIGS. 6-8** show a method of manufacturing a stent made in accordance with the present invention using a fixture mandrel to regulate flow.

[0019] **FIG. 9** shows an alternate embodiment of a method of applying a coating to a stent.

[0020] **FIG. 10** shows yet another alternate embodiment of a method of applying a coating to a stent.

DETAILED DESCRIPTION OF THE INVENTION

[0021] The stent with an eccentric coating of the present invention provides a coating having a different coating thickness on the stent outer diameter and stent inner diameter, i.e., an eccentric coating. The eccentric coating can be the primary carrier for a drug or other therapeutic agent. The eccentric coating can be thicker on the stent outer diameter to supply more drug to the vessel wall in which the coated stent is deployed and less drug to the vessel lumen. In one embodiment, a cap coating can be disposed on the eccentric coating to protect the eccentric coating, control the elution rate from the eccentric coating, provide an additional drug carrier, or provide combinations thereof. The eccentric coating can be applied by spraying a coating liquid on the stent outer diameter with a fixture mandrel interior to the stent to regulate the spray to the stent inner diameter.

[0022] **FIG. 1** shows a stent delivery system made in accordance with the present invention. The stent delivery system **100** includes a catheter **105**, a balloon **110** operably attached to the catheter **105**, and a stent **120** disposed on the balloon **110**. The balloon **110**, shown in a collapsed state, may be any variety of balloons capable of expanding the stent **120**. The balloon **110** may be manufactured from any sufficiently elastic material such as polyethylene, polyethylene terephthalate (PET), nylon, or the like. In one embodiment, the balloon **110** may include retention means **111**, such as mechanical or adhesive structures, for retaining the stent **120** until it is deployed. The catheter **105** may be any variety of balloon catheters, such as a PTCA (percutaneous transluminal coronary angioplasty) balloon catheter, capable of supporting a balloon during angioplasty.

[0023] The stent **120** may be any variety of implantable prosthetic devices capable of carrying a coating known in the art. In one embodiment, the stent **120** may have a plurality of identical cylindrical stent segments placed end

to end. Four stent segments **121**, **122**, **123**, and **124** are shown, and it will be recognized by those skilled in the art that an alternate number of stent segments may be used. The stent **120** includes at least one cap coating **125**, which can be applied to the stent **120** by dipping or spraying the stent **120** with a coating liquid, or applying the coating liquid with a combination of methods. The cap coating **125** can be applied as a liquid polymer/solvent matrix. A therapeutic agent can be incorporated in the cap coating **125**, or can be omitted and the cap coating **125** included for its mechanical properties alone.

[0024] An eccentric coating **130** between the cap coating **125** and the stent **120** is the primary carrier for a therapeutic agent. The cap coating **125** can be applied as a liquid containing the drug or other therapeutic agent dispersed in a polymer/solvent matrix.

[0025] The cap coating **125** and eccentric coating **130** are merely exemplary, and it should be recognized that other coating configurations, such as multiple coating layers, are possible. Although the cap coating **125** and the eccentric coating **130** are shown schematically on the outer circumference of the stent **120**, the cap coating **125** and the eccentric coating **130** can coat the whole stent **120**, both inside and outside, and around the cross section of individual stent wires. In another embodiment, the eccentric coating **130** can be present on a portion of the stent **120** without a cap coating **125** on that same portion.

[0026] The cap coating **125** and eccentric coating **130** can be a polymer including, but not limited to, urethane, polyester, epoxy, polycaprolactone (PCL), polymethylmethacrylate (PMMA), PEVA, PBMA, PHEMA, PEVAc, PVAc, Poly N-Vinyl pyrrolidone, Poly (ethylene-vinyl alcohol), combinations of the above, and the like. Suitable solvents that can be used to form the liquid coating include, but are not limited to, acetone, ethyl acetate, tetrahydrofuran (THF), chloroform, N-methylpyrrolidone (NMP), combinations of the above, and the like. Suitable therapeutic agents include, but are not limited to, antiangiogenesis agents, antiendothelin agents, antimitogenic factors, antioxidants, antiplatelet agents, antiproliferative agents, antisense oligonucleotides, antithrombogenic agents, calcium channel blockers, clot

dissolving enzymes, growth factors, growth factor inhibitors, nitrates, nitric oxide releasing agents, vasodilators, virus-mediated gene transfer agents, agents having a desirable therapeutic application, combinations of the above, and the like. Specific example of therapeutic agents include abciximab, angiopeptin, colchicine, eptifibatide, heparin, hirudin, lovastatin, methotrexate, rapamycin, streptokinase, taxol, ticlopidine, tissue plasminogen activator, trapidil, urokinase, and growth factors VEGF, TGF-beta, IGF, PDGF, and FGF.

[0027] **FIG. 2** shows a coated stent made in accordance with the present invention. The stent **150** comprises a number of segments **160**. The pattern of the segments **160** can be W-shaped or can be a more complex shape with the elements of one segment continuing into the adjacent segment. The stent **150** can be installed in the stent delivery system of **FIG. 1** for implantation in a body lumen.

[0028] Referring to **FIG. 2**, the stent **150** is conventional to stents generally and can be made of a wide variety of medical implantable materials, such as stainless steel (particularly 316-L stainless steel or 316LS), nitinol, tantalum, ceramic, nickel, titanium, aluminum, polymeric materials, tantalum, MP35N, titanium ASTM F63-83 Grade 1, niobium, high carat gold K 19-22, and combinations thereof. The stent **150** can be formed through various methods as well. The stent **150** can be welded, laser cut, molded, or consist of filaments or fibers which are wound or braided together in order to form a continuous structure. Depending on the material, the stent can be self-expanding, or be expanded by a balloon or some other device. The cap coating and eccentric coating can be on the surface of the segments **160**.

[0029] **FIG. 3** shows a cross section of a coated stent made in accordance with the present invention. A plurality of stent wires **170** are provided with a cap coating **125** and eccentric coating **130**. The stent wires form the segments, which form the stent. Although the cross section of the stent wires **170** is shown as generally rectangular with rounded corners, the cross section can be any number of shapes, for example and without limitation, those

shown in **FIGS. 4A, 4B, 4C** and **4D**, depending on fabrication methods, materials, and desired effect.

[0030] **FIGS. 4A, 4B, 4C** and **4D**, in which like elements share like reference numbers with **FIG. 3**, show examples of cross sections of stent wires with eccentric coatings made in accordance with the present invention. The cross sections can be of any number of other shapes depending on fabrication methods, materials, and desired effect. Please note, this is a representation only of the relative eccentricity of the stent coating – the actual stent cross section will vary depending on the type of stent used. An eccentric coating **130** is disposed on the stent wire **170** and a cap coating **125** can be disposed on the eccentric coating **130**. The eccentric coating **130** can comprise a first eccentric portion **131** positioned on the surface of the stent directly defining the inner lumen of the stent, i.e disposed towards the inner diameter of the stent and a second eccentric portion **132** positioned on the outer surface of the stent, i.e. disposed towards the outer diameter of the stent. The cap coating **125** can comprise a first cap portion **126** towards the stent inner diameter and a second cap portion **127** towards the stent outer diameter. In an alternate embodiment, the cap coating can be omitted and the eccentric coating provided as the outer layer of the stent.

[0031] The eccentric coating **130** can be the primary carrier of the therapeutic agent or drug. To concentrate the therapeutic agent at the vessel wall, rather than the vessel lumen, the second eccentric portion **132** can be thicker and have a greater volume than the first eccentric portion **131**. In an alternate embodiment, the second eccentric portion **132** can be thinner and have a lesser volume than the first eccentric portion **131** to concentrate the therapeutic agent at the vessel lumen for dispersion in the blood.

[0032] The cap coating **125** can be used for a number of purposes, including, but not limited to, a diffusion barrier to control the elution rate of the therapeutic agent from the eccentric coating **130**; a protective barrier to prevent damage to the eccentric coating **130**; a drug carrier for the same drug as the eccentric coating **130** or a different drug; a lubricating layer to reduce friction,

or a binding layer to increase friction, between the stent and the balloon of the stent delivery system; or various combinations thereof. In one embodiment, the cap coating **125** can be of a single material and uniform thickness to form a concentric cap coating. Such a uniform coating can be produced by dipping the stent in a liquid coating. In another embodiment, the first cap portion **126** and second cap portion **127** can be of different thicknesses or of different materials to provide a number of useful combinations. For example, the second cap portion **127** can be thicker than the first cap portion **126**, paralleling the relative thickness of the second eccentric portion **132** and the first eccentric portion **131**, respectively. In another example, the second cap portion **127** can be rapidly biodegradable, while the first cap portion **126** is non-biodegradable, so that the vessel wall is exposed to the second eccentric portion **132** and the drug eluting therefrom, but the first cap portion **126** limits drug elution from the first eccentric portion **131** into the vessel lumen. In another example, the second cap portion **127** can be made of one polymer-drug combination of benefit to and compatible with the vessel wall and the first cap portion **126** made of a different polymer-drug combination beneficial to and compatible with the blood stream. In another example, the second eccentric portion **132** is of greater thickness than the first eccentric portion **131**, and the first cap portion **126** is of greater thickness than the second cap portion **127**, allowing for greater release of drug to the vessel wall while inhibiting drug release into the vessel lumen. Those skilled in the art will appreciate that many useful combinations of the first cap portion **126** and the second cap portion **127**, not limited to the examples presented herein, are possible. Additionally, in cases where the cap coating **125** incorporates a drug, a protective, or "sacrificial," biodegradable coating may be applied over the cap coating **125** to protect the cap coating **125** and the underlying eccentric coating **130** from damage during handling or deployment of the stent.

[0033] **FIG. 5** shows a method of manufacturing a coated stent made in accordance with the present invention. At **180**, a stent is provided. A first polymer and drug (or other therapeutic agent) are mixed with a first solvent to

form a polymer/drug solution **182**. The polymer/drug solution is applied to the stent in an eccentric layer **184** and the eccentric layer cured to form an eccentric coating **186**. A second polymer is mixed with a second solvent to form a polymer solution **188**. The polymer solution is applied to the eccentric coating in a cap layer **190** and the cap layer cured to form a cap coating **192**. With reference to **FIG. 5**, the use of the terms "polymer," "solvent" and "drug" in the singular shall, in each case, include them in the plural (i.e., mixtures of one or more polymers, solvents and/or drugs).

[0034] Those skilled in the art will appreciate that the method of manufacturing can be varied for the materials used and the results desired. For certain polymer/drug solutions and polymer solutions, the curing step can be omitted or can be a simple drying process. In another embodiment, the first polymer and first solvent can be the same combination as the second polymer and second solvent. In yet another embodiment, the polymer solution can also contain a drug or other therapeutic agent.

[0035] **FIGS. 6-8** show a method of manufacturing a coated stent made in accordance with the present invention using a fixture mandrel to regulate flow. Referring to **FIG. 6**, a coating fixture **198** holds a stent while the coating is applied. The coating fixture **198** comprises a fixture mandrel **200** held in place by retainers **202**. The sloping face **204** helps to center and secure the stent during the coating operation. At least one of the retainers **202** can be attached to a drive (not shown) to rotate the stent in a single direction, or back and forth, during the coating operation. The drive can also provide axial movement if desired.

[0036] The fixture mandrel **200** can be held between the sloping faces **204** of the retainers **202**, or can be fixed to the retainers **202** by threads or other means. At least one of the retainers **202** can be detachable from the retainers **202** to allow installation of the stent to be coated between the retainers **202**. The fixture mandrel **200** can be metal or other material to block or redirect spray directed at the stent. The fixture mandrel **200** can be perforated to allow a portion of the spray to pass through the fixture mandrel **200**. The fixture

mandrel **200** can be made of a sponge-like material or have a sponge-like outer coating to retain spray directed at the stent.

[0037] **FIG. 7**, in which like elements share like reference numbers with **FIG. 6**, shows a stent mounted on the coating fixture. The coating fixture **198** holds a stent **210** for application of the coating from spray nozzle **212**. To apply the coating over the whole stent **210**, the spray nozzle **212** can be attached to a drive (not shown) to move the spray nozzle **212** relative to the coating fixture **198**. The spray rate from the spray nozzle **212**, the movement of the spray nozzle **212**, and movement of the coating fixture **198** can be controlled by computerized numerically controlled machines to control the coating pattern and thickness on the stent **210**. The stent **210** can be a bare frame of metal or other stent base materials, or can be a stent with one or more coatings previously applied. Alternatively, the stent **210** and coating fixture **198** can move relative to a stationary spray nozzle **212**, or both the stent **210**/ coating fixture **198** and the spray nozzle **212** can move relative to one another.

[0038] **FIG. 8**, in which like elements share like reference numbers with **FIG. 6 & 7**, shows a cross section of a stent mounted on the coating fixture during coating application. The spray nozzle **212** directs a spray **214** toward the stent **210**. The stent outer diameter **216** receives the full spray **218**. The fixture mandrel **200**, as well as the struts or wires of the stent **210** themselves, blocks a portion of the spray, so that the stent inner diameter **220** receives a shadow spray **222**. The spray rate difference between the full spray **218** and the shadow spray **222** results in a thicker coating on the stent outer diameter **216** than the stent inner diameter **220**, i.e., an eccentric coating. The stent **210** can be rotated in a single direction or in alternating directions to achieve coating characteristics as desired, depending on the coating materials used. The fixture mandrel **200** can optionally rotate with the stent.

[0039] The fixture mandrel **200** is shown as circular for purposes of illustration, but can be other shapes as desired. The fixture mandrel **200** can be perforated to allow spray to pass through the fixture mandrel **200** and reduce the

spray rate difference between the full spray **218** and the shadow spray **222**. In another embodiment, the fixture mandrel **200** can be made of or coated with a sponge-like material to partially retain the spray and to reduce splatter from the surface of the fixture mandrel **200**. In yet another embodiment, the cross section of the fixture mandrel **200** can vary axially to vary the coating eccentricity of the coating with axial position. For example, the middle of the fixture mandrel can have a larger cross section to make the coating more eccentric (more coating on the stent outer diameter) at the middle of the stent, allowing a greater drug loading in the middle. Similarly, the ends of the fixture mandrel can be wider to make the coating more eccentric at the ends of the stent. In other embodiments a specific, uniform degree of eccentricity of the coating along the longitudinal axis of the stent can be determined by setting a specific, uniform cross section of the fixture mandrel.

[0040] **FIG. 9** shows an alternate embodiment of a method of applying a coating to a stent. The spray nozzle **250** directs a spray **252** toward the stent **254**. The stent **254** can be a bare frame of metal or other stent base materials, or can be a stent with one or more coatings previously applied. The stent outer diameter **256** receives the full spray **258**. The stent outer diameter **256** blocks a portion of the spray, so that the stent inner diameter **260** receives a shadow spray **262**. The spray rate difference between the full spray **258** and the shadow spray **262** depends on the geometry between the spray nozzle **250** and the stent outer diameter **256**, including the proximity of the spray nozzle to the outside diameter and the size of the spray nozzle aperture.

[0041] In one embodiment, where the stent outer diameter **256** blocks a substantial portion of the spray, the spray rate difference between the full spray **258** and the shadow spray **262** results in a thicker coating on the stent outer diameter **216** than the stent inner diameter **220**, i.e., an eccentric coating. In another embodiment, where the stent outer diameter **256** blocks little of the spray, the spray rate difference between the full spray **258** and the shadow spray **262** results in substantially equal coating thicknesses on the stent outer diameter **216** and the stent inner diameter **220**, i.e., a uniform coating. The stent **210** can

be rotated by fixture rollers **264** in a single direction or in alternating directions to achieve coating characteristics as desired, depending on the coating materials used. The fixture rollers **264** can be used alone or can be used in conjunction with the retainers described in **FIG. 7.**

[0042] **FIG. 10** shows yet another alternate embodiment of a method of applying a coating to a stent. A pad carrying the liquid coating and disposed about a transfer roller transfers the liquid coating to the stent **270**. The stent **270** can be a bare frame of metal or other stent base materials, or can be a stent with one or more coatings previously applied. To coat the stent inner diameter **272**, inner pad **274** disposed about inner transfer roller **276** rotates against the inner diameter of the stent **270**. Typically, the inner transfer roller **276** and stent **270** can rotate in the same direction, but for certain stent and pad finishes, and liquid coating consistencies, the transfer roller **276** and stent **270** can rotate in opposite directions. To coat the stent outer diameter **278**, the outer pad **280** disposed about outer transfer roller **282** rotates against the outer diameter of the stent **270**. Typically, the outer transfer roller **282** and stent **270** can rotate in the opposite directions, but for certain stent and pad finishes, and liquid coating consistencies, the transfer roller **276** and stent **270** can rotate in opposite directions.

[0043] Although **FIG. 10** provides the example of applying the liquid coating to the stent inner and outer diameters simultaneously, the stent inner diameter and stent outer diameter could be coated in different steps. For example, the stent outer diameter can be coated to one thickness with one liquid coating, cured as necessary, and then the stent inner diameter coated with a different liquid coating to a different thickness. In another embodiment, the stent outer diameter could be coated with a biodegradable coating and the stent inner diameter could be coated with a non-biodegradable coating. This could allow the cap coating near the vessel wall to degrade quickly to permit underlying therapeutic agents to work at the vessel wall, while reducing the therapeutic agents entering the blood. Those skilled in the art will appreciate

that many combinations of stent inner and outer diameter coating thicknesses, therapeutic agents, and coating materials can be used to advantage as desired.

[0044] It is important to note that **FIGS. 1-10** illustrate specific applications and embodiments of the present invention, and is not intended to limit the scope of the present disclosure or claims to that which is presented therein. For example, the cap coating and eccentric coating can be applied in a variety of conventional ways, including painting, spraying, dipping, wiping, electrostatic deposition, vapor deposition, epitaxial growth, combinations thereof, and other methods known to those of ordinary skill in the art. The means of applying the liquid coating, such as spray nozzles or pads, can be moved in various paths relative to the stent to achieve particular patterns and thickness variations. Upon reading the specification and reviewing the drawings hereof, it will become immediately obvious to those skilled in the art that myriad other embodiments of the present invention are possible, and that such embodiments are contemplated and fall within the scope of the presently claimed invention.

[0045] While the embodiments of the invention disclosed herein are presently considered to be preferred, various changes and modifications can be made without departing from the spirit and scope of the invention. The scope of the invention is indicated in the appended claims, and all changes that come within the meaning and range of equivalents are intended to be embraced therein.